In the Specification:

Please amend the paragraph beginning at page 5, line 2 of the specification as follows:

Figures 1A-1D show ~~Figure 1 shows~~ T-cell responses in spleen to an intranasal Pa vaccine adjuvanted with LT-K63. The T-cell stimulus used in the assay was: PT (filled), FHA (diagonal shading), or B. pertussis bacteria (horizontal lines). Pa vaccine (FHA+rPT) was delivered with or without LT-K63 adjuvant, with or without light halothane anaesthesia. PBS was a control.

Please amend the paragraph beginning at page 5, line 6 of the specification as follows:

Figures 2A-2L show ~~Figure 2 shows~~ similar data for LT-R72 adjuvant, in (2A-2D ~~A~~) spleen (2E-2H ~~B~~) thoracic lymph node (2I-2L ~~C~~) superficial cervical lymph node. PMA/CD3 (no shading) was used as a positive control.

Please amend the paragraph beginning at page 5, line 8 of the specification as follows:

Figures 3A-3D show ~~Figure 3 shows~~ antibody responses for the same vaccines. Figures 3A and 3B show ~~Figure 3A shows~~ results using LT-K63 adjuvant ~~LT-K63adjuvant~~, and 3C and 3D show ~~3B shows~~ results using LT-R72 adjuvant. Filled bars show anti-PT responses; empty bars show anti-FHA responses.

Please amend the paragraph beginning at page 5, line 11 of the specification as follows:

Figures 4A-4D show ~~Figure 4 shows~~ the effect of toxin dose on the adjuvant effect of the mutant LT adjuvants.

Please amend the paragraph beginning at page 5, line 16 of the specification as

follows:

Figures 6A-6B show ~~Figure 6 shows~~ the IgA and IgG responses against the five antigens in a DTPa vaccine, comparing (i) alum adjuvant and intramuscular administration (empty bars) and (ii) LT-K63 adjuvant and intranasal administration (filled bars).

Please amend the paragraph beginning at page 5, line 19 of the specification as follows:

Figures 7A-7D compare ~~Figure 7 compares~~ T-cell responses for the same vaccines as shown in Figures 6A-6B ~~Figure 6~~.

Please amend the paragraph beginning at page 5, line 21 of the specification as follows:

Figures 9A-9C show ~~Figure 9 shows~~ T-cell proliferation (measured as ^{3}H-CPM) against the D (9C ~~bottom~~), T (9B ~~middle~~) and Pa (9A ~~top~~) components of DTPa vaccines administered using 5 different prime and boost regimens.

Please amend the paragraph beginning at page 5, line 24 of the specification as follows:

Figures 10A-10C show ~~Figure 10 shows~~ the T-cell cytokine responses against the Pa component of the vaccines of Figures 9A-9C ~~Figure 9~~.

Please amend the paragraph beginning at page 5, line 26 of the specification as follows:

Figures 11A-11C show ~~Figure 11 shows~~ the T-cell cytokine responses against the D component of the vaccines of Figures 9A-9C ~~Figure 9~~.

Please amend the paragraph beginning at page 6, line 1 of the specification as follows:

Figures 12A-12C show ~~Figure 12 shows~~ the T-cell cytokine responses against the T component of the vaccines of Figures 9A-9C ~~Figure 9~~.

Please amend the paragraph beginning at page 6, line 3 of the specification as follows:

Figures 13A-13B show ~~Figure 13 shows~~ serum IgG (13A ~~top~~) and lung homogenate IgA (13B ~~bottom~~) titres (log10) in response to the five defined antigens in the DTPa mixture.

Please amend the paragraph beginning at page 7, line 20 of the specification as follows:

The first vaccine (Figures 1A-1D ~~Figure 1~~) was adjuvanted with LT-K63 (10 μg/dose), whereas the second vaccine (Figures 2A-2L ~~Figure 2~~) was adjuvanted with LT-R72 (1 μg/dose). A control vaccine consisted of FHA + rPT only. The adjuvants were prepared as described in references 24 and 25.

Please amend the paragraph beginning at page 7, line 23 of the specification as follows:

Mice were immunized at 0 and 4 weeks either with the vaccine dose resuspended in 25 μl and applied to the external nares with a micropipette or, following light halothane anesthesia, with the vaccine dose resuspended in 50 μl and applied to the external nares with a micropipette. T-cell responses to killed *B. pertussis*, heat-inactivated PT and FHA were measured in spleen and thoracic and cervical lymph nodes at 6 weeks (Figures 1A-1D and 2A-2L ~~1 & 2~~).

Please amend the paragraph beginning at page 8, line 6 of the specification as follows:

Figures 3A-3D show ~~Figure 3 shows~~ that the mutant LT adjuvants also enhanced local and systemic antibody production following intranasal delivery of Pa.

Immunization with the control generated weak and inconsistent anti-PT and anti-FHA serum IgG and lung IgA responses. In contrast, formulation of the same antigens with LT-R72 or LT-K63 resulted in consistently strong serum IgG and lung IgA specific for PT and FHA and also significantly enhanced IgA responses, especially when the vaccine was administered under anaesthesia.

Please amend the paragraph beginning at page 8, line 22 of the specification as follows:

In experiments that directly compared the adjuvanticity of the toxins in vivo, BALB/c mice were immunized with Pa formulated with 1 or 10 μg of LTK63 or LTR72 as adjuvant, and the resulting immune responses were assessed (Figures 4A-4D ~~Figure 4~~). Intranasal immunization with control Pa generated weak T-cell responses, whereas addition of 1 μg LTK63 enhanced proliferation, as well as IFN-γ and IL-5 production, by spleen cells and lymph nodes in response to FHA or killed *B. pertussis*. Increasing the dose to 10 μg LTK63 resulted in modest further enhancements of proliferation and IFN-γ production. 1.0 μg LTR72 selectively augmented Th2 responses, with elevated levels of antigen-induced IL-4 and IL-5 production compared with those observed with Pa alone. Wild-type LT (1.0 μg) also selectively enhanced IL-4 and IL-5 production, but the effect was not as dramatic as that observed with LTR72. Furthermore, the mice that received 1.0 μg LTR72 had significantly higher anti-FHA and anti-PT IgG and IgA antibody titres than those immunized using LTK63 or wild-type LT. Increasing the dose of LTR72 from 1.0 to 10 μg resulted in enhancement of IFN-γ levels and lower levels of IL-4 and IL-5.

Please amend the paragraph beginning at page 10, line 22 of the specification as follows:

The intranasal vaccine enhanced cellular and humoral immune responses to tetanus and diphtheria as well as pertussis antigens (Figures 6A-6B and 7A-7D ~~6 & 7~~). The levels of serum IgG using the intranasal vaccine were equivalent to those observed using the intramuscular vaccine, but the mucosal immunization advantageously enhanced

local IgA responses.

Please amend the paragraph beginning at page 11, line 25 of the specification as follows:

T-cell proliferation (Figures 9A-9C ~~Figure 9~~) was weak for all groups for spleen cells stimulated with the pertussis antigens *in vitro*. The cells did, however, proliferate in response to the positive control (PMA+CD3). Proliferation responses to tetanus toxoid *in vitro* were significantly stronger in intranasally-boosted mice (after intramuscular priming) when LT-K63 was used as adjuvant. The strongest *in vitro* proliferation against the diphtheria component was seen in the mice immunized intranasally twice.

Please amend the paragraph beginning at page 12, line 4 of the specification as follows:

Cytokine responses to pertussis antigens (Figures 10A-10C ~~Figure 10~~) showed both IL-5 and IFN-γ production in all groups, indicating priming of both Th1 and Th2 populations *in vivo*. IL-4 production was limited to groups immunized in the same way both times. Priming and boosting with the intranasal LT-K63 formulation seems to give a stronger Th2 response (higher IL-4 and IL-5) than the groups primed intramuscularly.

Please amend the paragraph beginning at page 12, line 9 of the specification as follows:

Cytokine responses against the diphtheria antigen (Figures 11A-11C ~~Figure 11~~) were restricted to IL-4 and IL-5, with little or no IFN-γ detected for any group. Intranasal boosting with DTPa thus results in the priming of Th2 cells in vivo. The strongest Th2 response was generated from the mice immunized intranasally twice with the LT-K63 adjuvant. In contrast, two intramuscular injections gave no detectable IL-4 or IL-5 responses in the spleen, nor any IFN-γ.

Please amend the paragraph beginning at page 12, line 14 of the specification as

follows:

Cytokine responses against the tetanus antigen (Figures 12A-12C ~~Figure 12~~) showed the production of IL-4, IL-5 and low levels of IFN-γ in all mice, indicating a mixed Th1/Th2 response. IL-4 and IL-5 levels were, however, significantly higher in groups boosted intranasally with the LT-K63 adjuvant, compared with the non-adjuvanted intranasal booster or the intramuscular booster. IgG responses against TT, DT and PTN (Figures 13A-13B ~~Figure 13~~) showed no significant differences in titres between the various groups. Anti-PT and anti-FHA titres were slightly higher in groups primed and boosted with DTPa intramuscularly than in groups boosted intranasally (with or without LT-K63 adjuvant). Anti-FHA IgG were not detected, although this is not in agreement with the results presented above. IgA levels (Figures 13A-13B ~~Figure 13~~) showed that intramuscular priming and intranasal boosting using the LT-K63 adjuvant generated similar titres for most antigens to intranasal priming and boosting, although anti-PT levels were significantly lower. Intranasal boosting without the LT-K63 adjuvant generated lower IgA levels, particularly for DHA and PTN.